NIH Strategies for Developing Vaccines and Therapeutics in a Public Health Emergency

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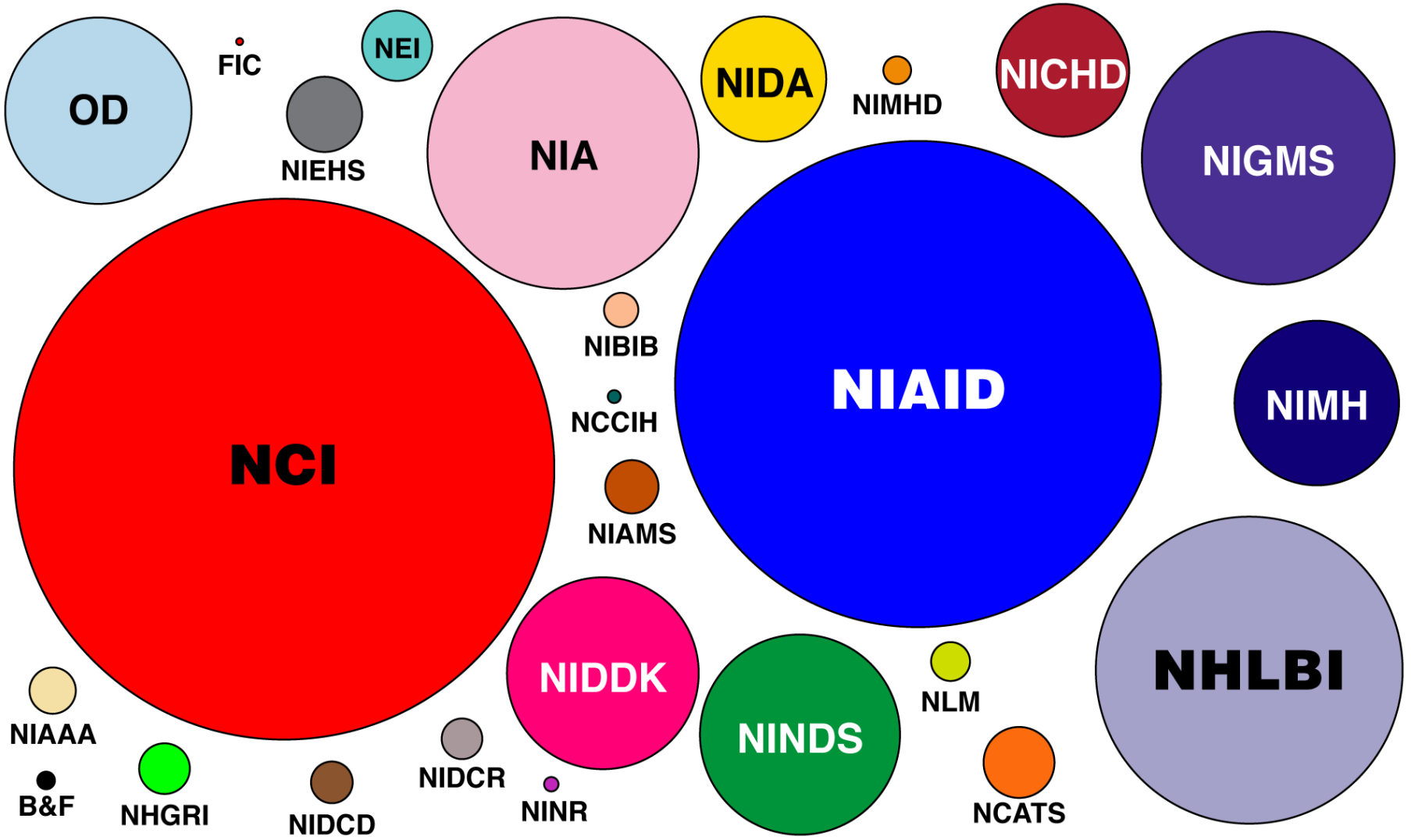
National Institute of Allergy and Infectious Diseases

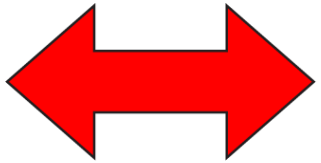
National Institutes of Health



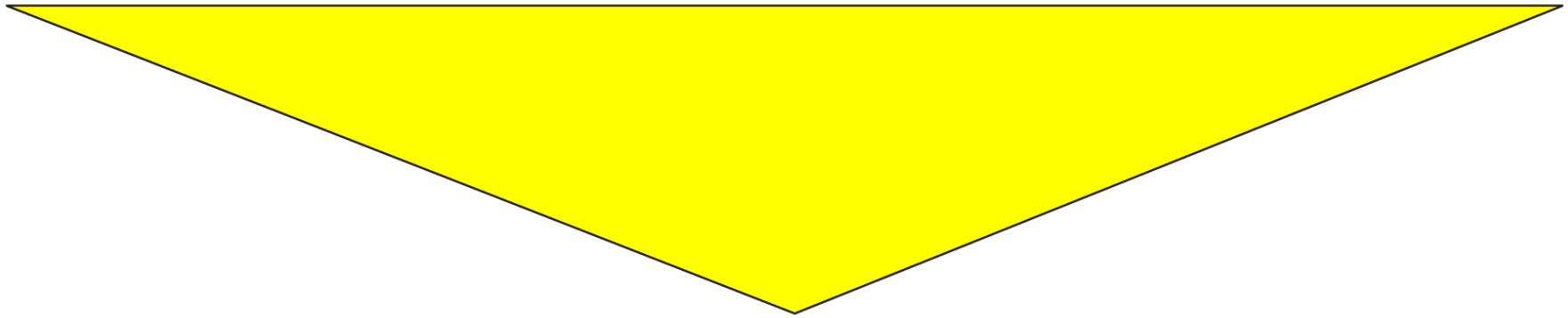
AS Fauci/NIAID

NIAID Research: A Dual Mandate

Maintain and "grow" a robust basic and applied research portfolio in microbiology, infectious diseases, immunology and immune-mediated diseases

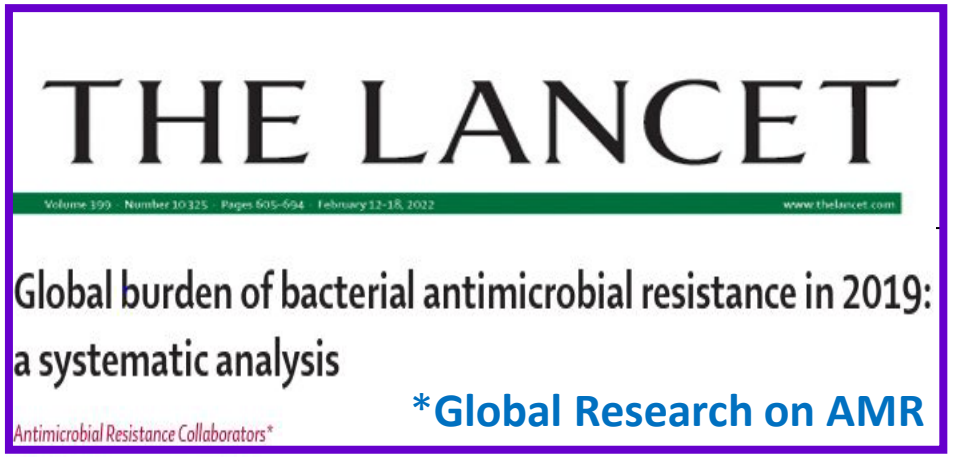


Respond rapidly to emerging and re-emerging disease threats

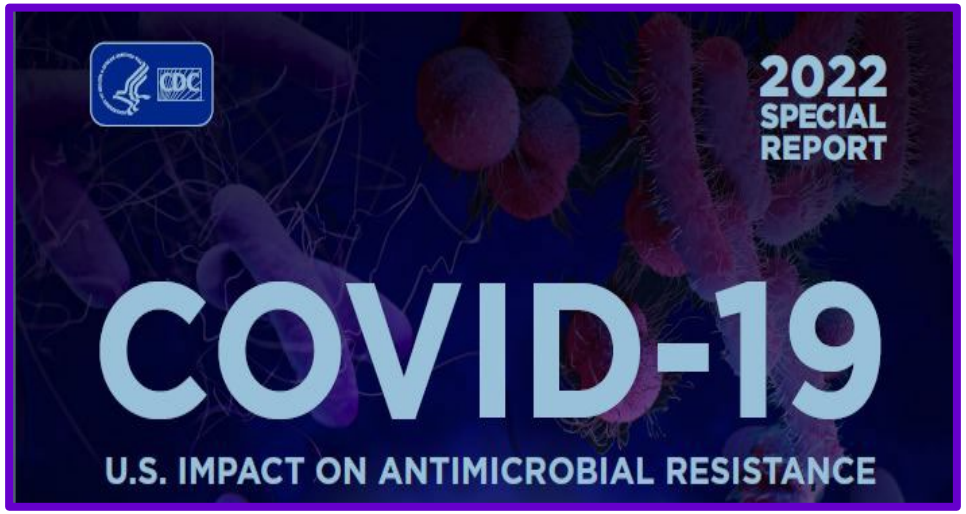


New/Improved Interventions

Current Antimicrobial Resistance (AMR) Threats



- **GRAM* Project** by Murray, C. et al. (2022)
  - Estimated deaths attributable to resistant bacteria are nearly equal to those from HIV and malaria combined
  - ESKAPE pathogens are among the top10 agents for AMR deaths (> 250K deaths in 2019)



- **CDC special report** on AMR infections during COVID-19 (2022)
  - 15% increase in AMR infections and deaths during hospitalizations in 2020 vs. 2019:
    carbapenem-resistant Acinetobacter, MDR-*Pseudomonas*, VRE, MRSA
  - 60% increase in antifungal resistance threat

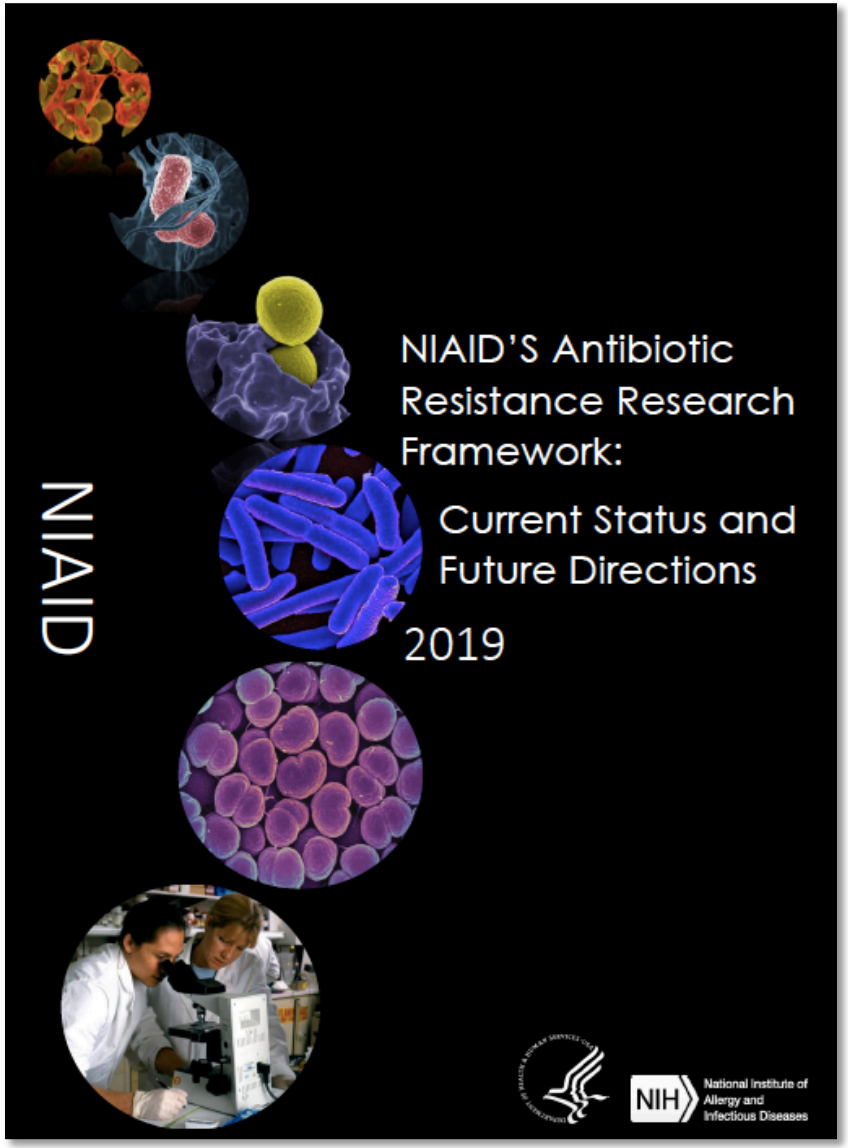
Importance of Non-Traditional Approaches during the Base Pandemic

- Limited antibiotics to treat infections due to AMR
- Difficult to develop antibiotics for gram (-) bacteria due to low permeability of cell wall and a variety of efflux pumps
- AMR outbreaks among vulnerable populations
  - ICU/ immunocompromised patients, nursing homes
  - Limitation of traditional antibiotic treatments
- R&D for alternatives encouraged by NIH:
  - Bacteriophage
  - Live biotherapeutics (a.k.a. Microbiome)
  - Vaccines and monoclonal antibodies

Vaccines for AMR

- **Indirect benefit**
  - Vaccine for respiratory viral infections
  - Influenza vaccine to prevent or reduce flu and unnecessary antibiotics for secondary infections
    (pneumonia & otitis media; reviewed in Klugman, K. *et al.* [2018] PNAS)
- **Direct benefit**
  - Pneumococcal vaccine to prevent pneumococcal pneumonia and to reduce antibiotic use
  - Challenges:
    - Uptake of vaccine in high-income countries
    - Availability of vaccine in low- and middle-income countries
    - Development of target vaccines for ESKAPE pathogens

NIAID Antibiotic Resistance (AR) Program



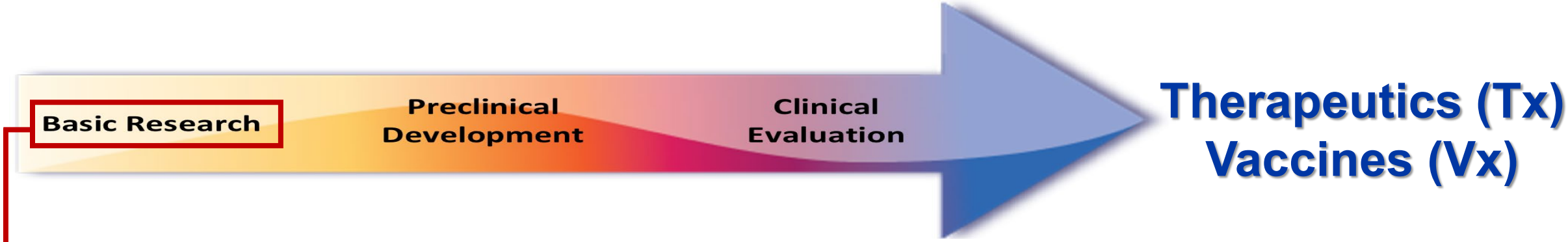
- **Basic Research**
- **Translational Research/ Product Development**
- **Clinical Research**

Diagnosis, Prevention and Treatment

https://www.niaid.nih.gov/sites/default/files/AR2019.pdf

NIH National Institute of Allergy and Infectious Diseases

NIAID Mechanisms to Support AMR Research



Investigator-Initiated

Targeted Initiatives
(R&D contracts)

- Model the host-pathogen molecular networks for gram (-) pathogens to identify more effective therapeutic targets
- Understand the mechanisms of phage biology

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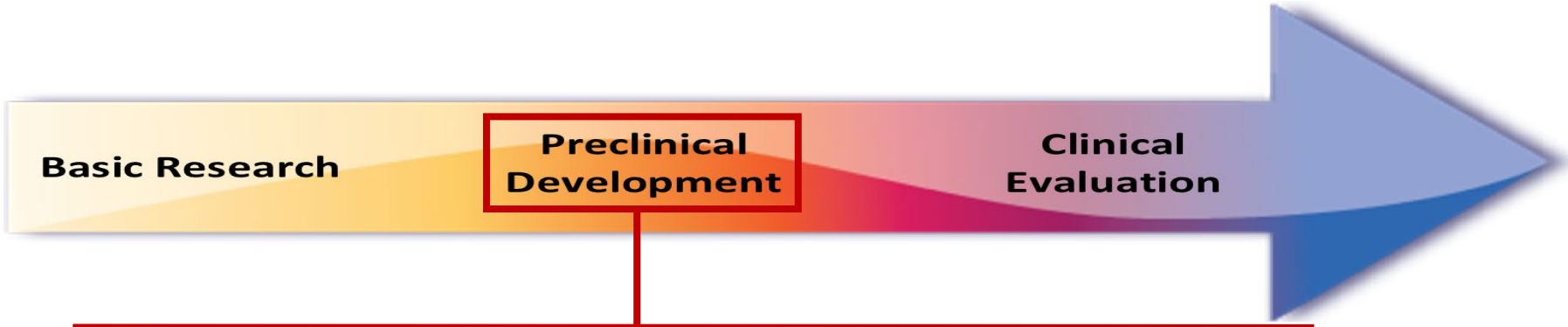

Tx
Vx

Grants/Product Development contracts

- Developing vaccine candidates for AMR Infections
- Improving technologies, for example, to make large-scale high titer phage preps

Research Resources

- Structural biology
- Genomics
- Bioinformatics
- BEI Resources Repository

Preclinical Service (PCS)

- Suite of free services contracts
- Animal model & assay development
- *In vivo* screening & efficacy testing (GLP)
- Chemical synthesis
- Vaccine testing & manufacturing (GMP)
- *In vitro* assessment of antimicrobial activity

NIAID Mechanisms to Support AMR Research

Phase I Clinical Trial Units*

- Assess safety of licensed and investigational therapeutic products
- CRS 3123 (an oral first-in-class antibiotic) study: safety, tolerability & PK in adult patients w/ *C. difficile* infection

Infectious Diseases Clinical Research Consortium (IDCRC)

- A network to evaluate Vx/Tx candidates against new threats (Phase 1-4)
- Bexsero Immunity Study (Phase II): assess mucosal immunity after Meningococcal group B vaccine to prevent Gonococcal infection

Antibacterial Resistance Leadership Group (ARLG)

- **ARLG 2.0 (2020-2026)**
- Develop, prioritize & implement a clinical research agenda to impact AR
- Phage clinical trial (Phase II): PK/PD in treating *P. aeruginosa* infection in Cystic Fibrosis patients

***Currently known as Early Phase Clinical Trial Units (EPCTU)**

Lessons Learned

- **Lessons learned during the COVID-19 pandemic:**
  - Prior scientific advances are essential for Tx/Vx development
  - Developing products is time-consuming
  - Mobilizing clinical trials in a timely manner is required
  - Expediting regulatory processes are needed
  - Global shortages in supply chain are encountered

- **What we can apply to the base pandemic:**
  - Sustaining research for priming the Tx/Vx development pipeline
  - Expediting screening of high probability compounds and vaccine candidates
  - Repurposing existing Tx
  - Leveraging existing clinical trial networks for new countermeasures and clinical research
  - Collaborating with other federal/global partners

Thank you

… For your interest